673

Lactic Esters by Reaction of Ammonium Lactate with Alcohols

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IN A previous publication from this laboratory (*2*), it was reported that ammonium and substituted ammonium salts of organic acids are capable of direct reaction with alcohols to produce the corresponding ester; ammonia or amine is the other product of reaction. Ammonium lactate was one of the salts that appeared promising in this novel type of reaction. This paper describes investigations in which this salt was used as a reactant with alcohols to prepare lactic esters.

Ammonium lactate appears to offer some important advantages as a raw material for preparing lactic esters. The steps in current practice for producing lactic esters are (*a*) fermentation of carbohydrates in the presence of calcium carbonate to produce a calcium lactate liquor; (*b*) acidification of the fermentation liquor to liberate lactic acid and simultaneously precipitate calcium sulfate; (*c*) filtration to remove calcium sulfate; and (*d*) esterification of the lactic acid with an alcohol. With ammonium lactate as the primary fermentation product, the steps leading to production of lactic ester are fermentation in the presence of ammonia to produce ammonium lactate, and reaction of ammonium lactate with an alcohol to form the lactic ester and ammonia; the ammonia then may be returned to the first step. Fermentation in the presence of ammonia has been shown by other investigators (*3, 4, 6*) to proceed satisfactorily, and the present study shows that esterification of ammonium lactate is also a satisfactory reaction. The apparent advantages of the process in which ammonium lactate is used as a raw material are: (*a*) elimination of the materials cost of calcium carbonate and sulfuric acid; (*b*) simplification of processing steps; (*c*) less difficulty because of corrosion; (*d*) the problem of disposing of large amounts of crude calcium sulfate would be avoided; and (*e*) the fermentation residue may have value as a by-product.

PREPARATION OF AMMONIUM LACTATE

This salt was prepared as follows: 80% edible grade lactic acid was diluted to approximately 20% concentration with water, and this diluted solution was heated on a steam bath for about 30 hours to convert the polylactic acid into monomeric lactic acid. The dilute lactic acid solution was then neutralized with concentrated ammonium hydroxide to a pH of 7 to 8 and the dilute ammonium lactate solution was concentrated in a steam-heated laboratory-size glass circulating evaporator (*5*) operated at 30 mm. of mercury pressure; the evaporation was discontinued when the temperature of the liquid reached approximately 80° C.

Because of the known explosion hazard resulting from mercury exposed to ammonia, the mercury manometer was open to the system only momentarily at the time the pressure was read. The concentrated ammonium lactate solution was withdrawn from the evaporator, and its pH, which was now approximately 6, was adjusted to 6.9 to 7.0.

The concentrated solution was analyzed for total nitrogen (*9*), and for ammonia nitrogen by the magnesium oxide method (*1*). The difference could be ascribed to nitrogen present as lactamide. The ammonium salt content was also checked by the formol titration method (*7*). In a typical run an ammonium lactate solution was obtained that contained 9.71% of total nitrogen and 9.61% of ammonia nitrogen; thus the salt was essentially free of lactamide. Formol titration showed the presence of 73.6% ammonium lactate, which was almost the same as the concentration of salt calculated by the nitrogen analysis. This solution was characterized as follows: n_D^{20}, 1.4499; d_4^{20}, 1.1962; viscosity at 20° C., 73.7 cs.

Obviously this preparation results in an ammonium lactate solution of high quality. For purposes of comparison in the reaction with butanol, a crude ammonium lactate solution was prepared by neutralizing a technical grade 55% lactic acid with ammonia to a pH of 6.60.

REACTION OF AMMONIUM LACTATE WITH ALCOHOLS

The reaction of ammonium lactate with alcohols was conducted by refluxing a mixture of ammonium salt and alcohol (mole ratio, 1 to 2.5) under conditions permitting continuous removal of both water and ammonia from the reaction mixture. This was conveniently accomplished by the use of an entraining agent, which in most cases was the alcohol used in the reaction. For water-soluble alcohols, toluene or some other suitable solvent was added as an entraining agent.

The reaction temperature ranged from 100 to 150° C. for the lower alcohols, and from 120 to 200° for the higher alcohols. In general the reaction required 5 to 10 hours for completion. After completion of the reaction, the mixture was washed with small portions of water, and the ester was isolated by distillation in vacuum. In some cases the reaction mixture was distilled without the preliminary washing treatment, and this method of isolation resulted in higher yields.

The lactic esters were easily isolated as pure materials by a single distillation through a Vigreux column and generally boiled within a 2° range. The identity and purity of the lactic esters were suitably indicated by boiling point and refractive index, which were in agreement with previously observed values. The yield and conversion data were based on the weight of ester isolated. Because iso-octyl alcohol is a mixture of alcohols, the yield of iso-octyl lactate (Expt. 11, Table I) was based on saponification of the lactate fraction.

Experimental Procedure. The reaction of ammonium lactate with butanol is typical of the esterification procedure. The apparatus used (Figure 1) was that commonly employed in esterification reactions. A mixture containing 150 grams of 71.3% ammonium lactate in aqueous solution and 185 grams of

TABLE I. REACTION OF AMMONIUM LACTATE WITH VARIOUS ALCOHOLS

Reaction mixture: 146 grams of 74% (1.0 mole) aqueous ammonium lactate and 2.5 moles of alcohol

Expt.	Alcohol	Toluene, Ml.	Temperature, ° C. Reaction[a]	Vapor[b]	Time, Hours	Conversion, % Lactic ester	NH_3
1	*n*-Butyl	None	106–134	111	7.0	49	87
2	*n*-Butyl	None	104–136	115	6.5	64[c]	85
3	*n*-Butyl[d]	None	105–142	118	4.0	67[c]	92
4	*n*-Butyl[e]	None	100–134	115	5.0	49	61
5	Isobutyl	100	82–100	112	7.0	43	82
6	*sec*-Butyl	100	101–111	95	13.0	12	74
7	Methallyl[f]	None	105–144	113	14.5	53	88
8	*n*-Hexyl[f]	None	119–179	157	5.0	73	87
9	Cyclohexyl[f]	None	119–179	157	5.0	55	84
10	Methyl isobutyl carbinol[f]	None	118–152	130	9.0	35	76
11	Iso-octyl[g]	None	132–198	178	0.8	65	85
12	*n*-Octyl	None	137–213	191	1.7	78	90
13	2-Ethylhexyl	None	122–201	175	5.0	75	85
14	Capryl	50	120–194	148	6.5	47	56
15	2-Ethoxyethyl	100	101–149	110	9.5	65[h]	61
16	Tetrahydrofurfuryl[f]	200	103–138	110	8.5	65[c]	83
17	Control: lactic acid (1.0 mole) + *n*-butyl alcohol (2.5 moles)	None	105–136	116	2.5	62[c]	..

[a] Initial and final temperature of refluxing reaction mixture.
[b] Temperature of refluxing vapor at conclusion of experiment.
[c] Ester distilled directly from reaction mixture.
[d] Reaction carried out under a Fenske column.
[e] Crude NH_4 lactate, from neutralizing crude lactic with NH_3, was used.
[f] NH_4 *p*-toluenesulfonate (0.05 mole) was included in reaction mixture.
[g] Commercial product. Properties of lactate: b.p. 78–85° C./0.9 mm.; n_D^{20}, 1.4374.
[h] Reaction mixture was washed with saturated NaCl, and organic layer was distilled.

n-butanol was refluxed in the reaction flask. Vapor from the refluxing reaction mixture was led through a 2-foot Vigreux and condensed above a moisture trap. The two-phase condensate collected in the trap; the upper alcohol layer was automatically returned to the reaction flask, and the lower aqueous layer containing some ammonia was periodically withdrawn. The noncondensable vapor was led into boric acid solution to absorb the remaining ammonia. The total ammonia was determined by titration (*8*). A safety trap, merely a reservoir, was essential to prevent the boric acid solution from being drawn back into the

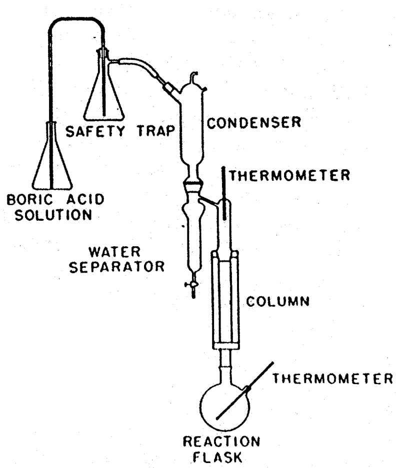

Figure 1. Apparatus for Esterification of Ammonium Lactate

reaction flask. After 6.5 hours, 66 ml. of water and 0.85 mole of ammonia were collected, and the esterification practically ceased, as indicated by the low rate of water formation as well as the rise in temperature of the refluxing vapor. The reaction temperature had risen from 104° to 136° C., the vapor temperature remained at approximately 90° until water formation ceased, when it gradually reached 115° C. The reaction mixture was washed with small portions of water, and the butyl lactate, boiling at about 75° at 10 mm., was isolated by distillation in vacuum. The conversion was approximately 50% (Table I, Expt. 1). When the ester was isolated by distillation without washing the reaction mixture, the recovery was considerably improved (conversion 65%, Expt. 2).

The reaction of ammonium lactate with various alcohols is summarized in Table I. The conversion to lactic ester was reasonably high, usually 50% or higher. Primary alcohols in general resulted in higher conversion to ester than did secondary alcohols. It also seems apparent that high boiling alcohols are more suitable in this reaction than low boiling alcohols of similar structure. *n*-Hexyl, *n*-octyl, and 2-ethylhexyl alcohols, all primary alcohols of high boiling point, gave the highest conversion to lactic ester, 73 to 75%. Conversion to ammonia was usually 80% or higher; the lower values for conversions in Table I may have been caused by mechanical losses of ammonia. Comparison of Experiments 2 and 3 (Table I) shows that when the reaction was carried out under an efficient column (Fenske helix-packed column), the time of reaction was considerably reduced and conversion to ester was slightly higher.

Apparently lactamide is not an intermediate in the reaction of ammonium lactate with alcohols; neither ester nor ammonia was formed when lactamide was refluxed with butanol under the same conditions that produced butyl lactate from ammonium lactate. The uncatalyzed esterification of lactic acid with butanol (Expt. 17) required approximately half the time of the ammonium salt reaction and gave similar conversion to ester. It seems likely that the reaction proceeds through dissociation of the ammonium lactate to ammonia and lactic acid and that the latter undergoes esterification with butanol.

$$CH_3CHOHCOONH_4 \rightleftharpoons CH_3CHOHCOOH + NH_3$$

$$CH_3CHOHCOOH + ROH \rightleftharpoons CH_3CHOHCOOR + H_2O$$

$$\text{Net: } CH_3CHOHCOONH_4 + ROH \rightleftharpoons CH_3CHOHCOOR + NH_3 + H_2O$$

The only observed by-products of the reaction were distillation residues, which consisted mainly of derivatives of polylactic acid; butyl lactyllactate was isolated from the distillation residue as the fraction following butyl lactate. Because the polylactic acid derivatives can be converted to the monomeric ester, yields of lactic ester presumably will be higher than the conversion figures in Table I. This was shown in the preparation of butyl lactate, discussed later, in which the by-products were recycled.

EFFECTS OF VARIABLES ON AMMONIUM LACTATE-BUTANOL REACTION

Salt-Alcohol Ratio. Table II shows the effect of the ratio of alcohol to ammonium lactate on conversion to butyl lactate. Increasing this ratio increased the conversion to butyl lactate. A ratio of 2.5 moles of butanol to 1 of ammonium salt appeared to be as practical as the higher ratio. The low conversion to monomeric lactic ester when the alcohol salt ratio was below one is attributed to the formation of esters of polylactic acid.

TABLE II. EFFECT OF RATIO OF BUTANOL TO AMMONIUM LACTATE ON CONVERSION TO BUTYL LACTATE

Ratio[a]	Toluene, Ml.	Temperature, ° C. Reaction[b]	Vapor[c]	Time, Hours	Conversion, % Butyl lactate	NH_3
0.5	50	112–185	104	7.0	14	65
1.0	50	100–183	102	5.0	33	43
2.5	None	104–137	114	6.0	53	85
5.0	None	104–126	116	5.5	59	87

[a] Ratio of alcohol to ammonium lactate.
[b] Initial and final temperature of refluxing reaction mixture.
[c] Final temperature of refluxing vapor.

TABLE III. PREPARATION OF BUTYL LACTATE FROM AMMONIUM LACTATE RECYCLING EXPERIMENTS

Cycle	Ammonium Lactate Moles	Temperature, ° C. Reaction[a]	Vapor[b]	Time, Hours	Ester, Moles	NH_3, Moles
Series A						
1	1.00	104–134	115	5.5	0.58	0.75
2	1.00	105–139	115	5.5	0.82	0.79
3	1.00	109–146	114	3.5	0.77	0.75
4	1.00	112–150	115	4.0	0.93	0.86
5	1.00	112–149	115	4.0	0.82	0.72
6	1.00	112–157	114	4.0	0.91	0.79
7	1.00	112–151	114	3.5	0.86	0.71
8	1.00	113–157	114	4.0	0.88	0.74
9	1.00	113–152	112	4.0	0.90	0.76
Total	9.00				7.47	6.87
Over-all yield: butyl lactate, 83%; NH_3, 75%.						
Series B						
1	1.00	104–136	115	6.5	0.64	0.85
2	0.64	108–172	115	3.5	0.49	0.55
3	0.49	108–140	115	4.0	0.50	0.48
4	0.50	108–144	114	6.5	0.54	0.46
5	0.54	107–140	115	5.5	0.53	0.53
6	0.53	108–155	113	4.0	0.46	0.46
7	0.46	108–159	113	2.5	0.36	0.37
Total	4.16				3.52	3.70

Over-all yield after seven cycles: butyl lactate, 85%; NH_3, 89%.

[a] Initial and final temperature of reaction mixture.
[b] Final temperature of refluxing vapor.

Catalysis Study. Because the reaction of ammonium lactate with butanol bears some resemblance to esterification, an attempt was made to accelerate this reaction with catalysts. Hence the reaction of ammonium lactate with butanol was conducted in the presence of 5 to 10 mole % of various salts and other reagents. Ammonium sulfate, ammonium *p*-toluenesulfonate, sodium acetate, and aluminum chloride did not show any catalytic activity. Boric acid, trihexylamine, basic aluminum acetate, and silica gel exerted some catalytic activity, reducing the time of reaction by approximately one half. Carrying out the reaction under an efficient column also reduced the reaction time (Expt. 3, Table I). The conversion to butyl lactate was not greatly affected by these various agents.

PREPARATION OF BUTYL LACTATE FROM AMMONIUM LACTATE—RECYCLING OF BY-PRODUCTS

The data in Table I show that the reaction of ammonium lactate with butanol results in approximately 50 to 60% conversion of the salt to butyl lactate. Because the probable by-products of this reaction are essentially esters of polylactic acid, it seemed likely that recycling the by-products would materially increase the yield. To obtain an estimate of the ultimate yield of butyl lactate from the reaction of ammonium lactate with butanol, a series of batch reactions was carried out in which the by-products (the distillation residues) were recycled. The reaction mixture after cycle 1 was composed of 1 mole of fresh ammonium lactate, 2.5 moles of fresh butanol and distillation residue (from the isolation of butyl lactate from the previous cycle). The reactions were conducted as described under "Experimental Procedure." The over-all yield was 7.47 moles of butyl lactate from 9.00 moles of ammonium lactate or 83% (Table III, series A). The, yield of ammonia, expected to be better than 85% from the data of Table I, was only 75% for some undetermined reason (perhaps the butanol fraction, which was not recycled, contained ammonia).

A similar series of recycling experiments was conducted in which the recovered butanol as well as by-products was used in the next cycle (Table III, series B). The reaction mixture, after the first cycle, comprised recovered butanol and distillation residue from the preceding cycle and fresh ammonium lactate and butanol (equivalent to the butyl lactate isolated in the previous cycle). In this instance the yield of both butyl lactate and ammonia was highly satisfactory—85 and 89%, respectively.

Presumably, in the reaction of ammonium lactate with other alcohols the yield of lactic ester would be high if the by-products of the reaction were recycled.

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The purpose of this investigation was to study the feasibility of a new reaction—namely, the reaction of an ammonium salt with alcohols—as a method of the preparation of lactic esters.

The reaction of ammonium lactate with various alcohols, particularly those containing four or more carbon atoms, was studied on a laboratory scale. The reaction bears some resemblance to direct esterification and the corresponding lactic ester and ammonia were produced in satisfactory yields. Both primary and secondary alcohols were suitable, although the former gave higher conversions to ester. *n*-Hexyl, *n*-octyl, and 2-ethylhexyl lactates were obtained in highest conversions (73 to 78%). Butyl lactate was produced in conversions of 65% per pass; however, by recycling the by-products of the reaction, an over-all yield of 85% of butyl lactate was obtained. Presumably, recycling of the by-products would be similarly advantageous in the preparation of other lactic esters.

Ammonium lactate, a primary fermentation product, appears to have some important advantages as a raw material for the production of lactic esters.